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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,513	01/30/2002	Judy Senior Pinsker	MAXIM.079C1	3651

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EXAMINER	
YOUNG, MICAH PAUL	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/066,513	Applicant(s) PINSKER, JUDY SENIOR	
	Examiner Micah-Paul Young	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Acknowledgment of Papers Received: Amendment and Response filed 09/08/03.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1, 3-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Allen (USPN 4,895,727 hereafter referred to as '727), Hellstrand (WO 97/42968 hereafter referred to as '968), Fisher (USPN 3,880,996 hereafter referred to as '996) and Popovich et al (USPN 4,673,385 here after referred to as '385). Claims 1 and 3-11 are drawn to a transmucosal dosage form comprising a histamine, solvent, gelling agents, other active agents, and an absorption enhancer. Claims 12-17 are drawn to a method of manufacturing the formulation of the invention.

'727 discloses a transmucosal formulation comprising histamine dihydrochloride (col. 6, lin. 5 – 13), therapeutic agents such as vitamins, and analgesics (col. 5, lin. 56 – 64). The formulation also comprises solvents, (water, ethyl alcohol) and swelling agents (methyl cellulose) (col. 6, lin. 57 – 66). The composition further comprises surfactants, such as polyvinyl pyrrolidone, and alcohols such as stearyl and isopropyl alcohol (*Id.*).

What is lacking in the reference is a disclosure of histamine phosphate in the formulation. '968 discloses a histamine formulation where the histamine has a synergistic relationship with cancer fighting agents. '968 phosphate is used by the formulation along with various carriers such as solvents, swelling agents, and penetration enhancers such as dimethylsulfoxide (pg. 18, lin. 8 – 13). A skilled artisan would be motivated to substitute the histamine of this reference into the transmucosal formulation of '727 with an expected result of a histaminic formulation that was easily dissolvable in the blood stream.

What is further lacking from both references is an expressed disclosure of the histamine composition as penetration enhancers. However, histamines would have this property inherently. Histamines are by definition vasodilating agents, meaning they open blood vessels allowing for more blood to flow. '996 and '385 disclose formulations where histamine dihydrochloride and phosphate are described as vasodilating agents. With this in mind, it would have been obvious to a skilled artisan that these agents (histamines, and their salts) would have been useful in the enhancing the penetration of any formulation in which they are present. The histamine compounds would upon contact with the mucosal membrane, inflame the blood vessel and cause an increase in blood flow to the area. At that point the active agents (vitamins, analgesics, etc.) would be more easily accepted and dissolved into the bloodstream, simply by the shear volume of blood. It is the position of the examiner that applicant ahs simply described an inherent feature of the compound in a new way. This new description does not impart patentability on the invention.

With regard to claims 1 and 6-8, which recites limitations to the concentrations of various components of the invention, it is the position of the examiner that these concentrations do not

impart patentability on the invention. These concentrations represent the optimize ranges which can be determine through routine experimentation. The art represents the general teaches of the combination of the components of the invention. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various cosmetic compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

With this in mind a skilled artisan would have been motivated to follow the teachings and suggestions in the art. A skilled artisan would have been motivated to substitute the histamine compounds of '986 in to the formulation in order to impart vasodilating properties on the formulation thereby increasing the permeation the other active agents. A skilled artisan would have followed the knowledge in the art as established by '996 and '385 that histamine salts such as dihydrochloride and phosphate can be used as and are classified as vasodilating agents. This knowledge would have served as motivation to the skilled artisan in creating a transmucosal (buccal, nasal, etc.) formulation where the formulation delivers its active agents more efficiently to the blood stream. A skilled artisan would have expected a transmucosal formulation with improved delivery of active agents such a vitamins and analgesics.

Response to Arguments

2. Applicant's arguments filed 10/16/03 have been fully considered but they are not persuasive. Since applicant was the first to discover the permeation enhancing properties of histamine and its agonists on drugs or vaccines, it is not obvious in light of the prior art. Contrary to applicant's claims, the use of histamine and histamine agonists as permeation enhancing agents transdermally is a well known property of histamine, as seen in Nahoum, histamine and histamine agonists are used to enhance the penetration of estrogen, testosterone and sex hormones through the skin and mucosa of sexual organs (abstract, examples). The histamine of Nahoum inherently has this permeation enhancement property, and would be present in any formulation. This would be present in the histamine present in the cited prior art combination of '727 and '968, with support from '996 and '385. Since the histamine of the this combination would naturally enhance the permeation of any active compounds associated with it, the specific histamine compounds of '996 and '385. Given this information, a skilled artisan would be motivated to optimize the concentrations in order to maximize the permeation and delivery of the active agents. For these reasons, the claims remain rejected.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

MP Young

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600